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EXAMINER

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/712,638
Filing Date: November 14, 2000
Appellant(s): RIGOUTSOS ET AL.

Michael J. Chang
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed October 26, 2004.

HL

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(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The amendment after final rejection, filed on March 05, 2004, for canceling claims 13-22, 24, and 26 has been entered.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct.

(7) *Grouping of Claims*

Appellant's brief includes a statement that claims 1-12, 23, and 25 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8). Appellant has claims 1-3, 10, 12, 23, and 25 stand or fall together. Claim 4, 5, 6, 7, 8, 9, or 11, respectively, stands or falls alone.

The appellant's statement in the brief that certain claims 1-12, 23, and 25 do not stand or fall together is not agreed with because claims 1-12 are directed to a method, while claims 23

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and 25 are directed to a system or apparatus. Therefore, the Examiner is noting that claims 23 and 25 do not stand or fall together with claims 1-12.

(8) *Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

Benson et al., Nucleic Acids Research, Volume 25, pages 1-6, 1997.

NCBI, NCBI NEWS, pages 1-18, August 1996.

Kleffe et al., Bioinformatics, Volume 14, pages 232-243, 1998.

Altschul et al., Journal of Molecular Biology, Volume 215, pages 403-410, 1990.

(10) *Grounds of Rejection*

The following ground(s) of rejection are applicable to the appealed claims:

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

1. Claims 4 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

BASIS FOR REJECTION

2. Specific to the limitation of “without using any knowledge about properties or features of sequences”, said limitation causes claim 4, which depends from claim 1, to be vague and indefinite because claim 1 recites “the sequences are not aligned.” The recitation of “the sequences are not aligned” in claim 1 has been reasonably construed as providing “knowledge

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about properties or features of sequences.” Therefore, the step of discovering without “knowledge about properties or features of sequences” in claim 4 is unclear since “knowledge about properties or features of sequences” has been previously provided in claim 1. Clarification of the metes and bounds is required.

3. Specific to line 2, the limitation of “unaligned sequences” causes claim 4 to be vague and indefinite because claim 1, line 2, from which claim 4 depends, recites “not aligned.” Claim 4 is unclear whether the limitations are the same. Further, the antecedent basis for said limitations are unclear because of the inconsistency of said limitations. Clarification of the metes and bounds is required.

4. Claim 7, lines 1-2, the limitation of “for one of the positions...one expected symbol is a plurality of expected symbols” causes said claim to be vague and indefinite because it is unclear whether “one of the positions” is occupied by one symbol or a plurality of symbols. Clarification of the metes and bounds is required.

RESPONSE TO ARGUMENTS

5. On pages 3-4, Appellant argues that the limitation of “discovering...in the set of unaligned sequences” is defined in the specification in such a way that the metes and bounds of claim 4 are clearly ascertainable. Appellant points to page 8, lines 6-7, and page 7, lines 19-25, to support that the argued limitation is not vague and indefinite. Appellant’s argument has been found to be unpersuasive because the pointed to support does not define the argued limitation in

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such a way that clearly points out and distinctly claims the subject matter which Appellant regards as the invention.

6. Specific to page 7, lines 19-23, Appellant points to the specification to argue that said page “sets forth the definition of a feature.” Further, Appellant points to page 7, lines 23-25, to argue that said page “defines property as” which is not persuasive because the pointed support discloses “an example of a feature.” An exemplary disclosure is not an explicit definition; therefore, the exemplary disclosure does not clearly define the argued limitation as asserted by Appellant. The exemplary disclosures do not clearly define the metes and bounds of the limitation of “discovering...in the set of unaligned sequences”; therefore, the claim as a whole is vague and indefinite.

7. Specific to the pointed support on page 8, lines 6-7, the disclosure supports that a type of feature of the sequences is derived from aligning the sequences. The same disclosure supports that “the sequences not aligned” is also a type of feature property. For example, one of skill in the art would expect two scenarios from discovering similarities (features) between sequences wherein each scenario supports the type of feature described in the instant specification. The first feature results from the sequences being aligned. The second feature results from the sequence being “not aligned” which represents sequences that are not similar.

8. On page 4, Appellant argues that the terms “unaligned” and “not aligned” are the same. Appellant further cites the Merriam-Webster’s Collegiate Dictionary, 10th edition, to define said terms. Appellant further argues, from the definitions, the term “unaligned” has been defined simply as “nonaligned,” e.g., the equivalent of “not aligned.” Appellant’s argument is not

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persuasive because the dictionary does not cite “not aligned” as being equivalent to unaligned, but rather ‘nonaligned.’ It is noted that “unaligned” could have the additional confusing interpretation of unaligning a previously aligned set of sequences.

9. On page 5, Appellant argues “the metes and bounds of claim 7 are ascertainable from the teachings of the claims and supporting specification.” Appellant’s argument is not persuasive because the pointed to support on pages 13 and 25 does not make clear whether “one of the positions” is occupied by one symbol or a plurality of symbols.

CLAIM REJECTIONS - 35 USC § 101

10. Claims 1-12, 23, and 25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory algorithm type subject matter.

11. The instant rejection is directed to the computer embodiment of the claimed invention.

BASIS FOR REJECTION

12. Claims 1-12 are rejected because said claims are directed to a method, system, and an article of manufacture comprising steps for analyzing sequence data without any physical alteration step, which is considered to be non-statutory subject matter. “For example, a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory.

However, a claimed process for digitally filtering noise employing the mathematical algorithm is statutory” (MPEP § 2106 (IV)(B)(2) (b), part ii). Similar to the nonstatutory example above, the instant invention comprises algorithmic steps for analyzing sequence data without any physical alteration resulted from said analysis.

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13. Specific to claims 23 and 25, it is noted that said claims are directed to a system and apparatus comprising computer-readable code. As recited in the claims, the computer-readable code has been reasonably interpreted as nonfunctional descriptive material because the descriptive material cannot exhibit any functional interrelationship with the way in which the computing processes are performed. For example, music stored in compact wherein the compact disc acts as nothing more than a carrier for the nonfunctional. Therefore, an invention directed to a compact disc comprising music is nonstatutory (MPEP § 2106 (IV)(B)(1) (b)). Similar to the example, the system and apparatus of claims 23 and 25 merely store the nonfunctional material, computer-readable code. Therefore, claims 23 and 25 are directed to nonstatutory subject matter.

RESPONSE TO ARGUMENTS

14. On page 6, Appellant argues “each of independent claims 1, 23, and 25 are expressly directed to a practical application. Appellant points to page 6, lines 1-3 and 14-15, to support that the claimed invention is directed to a practical application. Appellant’s argument and pointed support directed to claims 1-12, 23, and 25 are not persuasive as discussed below.

15. Claim 1 which is directed to method comprising steps for analyzing sequence data without any physical alteration step is considered to be non-statutory subject matter. “For example, a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory. However, a claimed process for digitally filtering noise employing the mathematical algorithm is statutory.” (MPEP § 2106 (IV)(B)(2) (b), part ii). The step of filtering noise is controlled by the results generated from the data manipulation. The difference between

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the claimed invention and the citation above is that the instant claims recite limitations directed to data manipulation without any limitation which could reasonably be construed as controlling any physical steps resulted from said data manipulation.

16. Specific to the pointed support to assert that the claimed method is directed to a practical application, it is noted that the claimed process merely comprises algorithmic steps for analyzing sequence data which does not result in any type of physical alteration as discussed. The MPEP § 2106 (IV)(B)(2) (b) requires that a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technological arts is either disclosed in the specification or would have been known to a skilled artisan, or (B) be limited to a practical application within the technological arts. The claimed method does not satisfy either one of the recited requirements; therefore, it is not statutory.

17. Specific to claims 23 and 25, it is noted that said claims are directed to a system and apparatus comprising computer-readable code. As discussed above, the system and apparatus of claims 23 and 25 merely store the nonfunctional material, computer-readable code. Therefore, claims 23 and 25 are directed to nonstatutory subject matter.

CLAIM REJECTIONS UNDER - 35 USC § 102

18. Claims 1-8, 10-12, 23 and 25 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Benson et al. (1997).

BASIS FOR REJECTION

19. Benson et al. discloses that the NCBI provides GenBank comprising over 600 million nucleotide bases, and a subset of GenBank is the UniGene collection of unique human gene sequences (Benson et al., page 1, column 2, Organization of the database §, and page 2, column 2, EST data §, lines 16-18).

20. The inclusion of NCBI News is not being used as prior art, but only to expand on the inherent characteristics of the UniGene Collection as cited by Benson et al. NCBI News discloses UniGene comprises clusters of EST sequences wherein said EST sequences are not complete and have not been characterized (unaligned) (NCBI News, page 3, lines 7-11), as in instant claim 4.

21. ESTs are screened against each other to determine those likely to be derived from the same gene and sequences share statistically significant DNA similarity (common patterns) are placed into the same cluster (NCBI News, page 3, lines 35-39), as in instant claim 5.

22. One important use of the UniGene clusters (set of sequences) is to identify novel and non-redundant sequence candidates that identify coding sequences in the genome based on predetermined patterns of said clusters (NCBI News, page 3, lines 1-35), as in instant claims 1-3.

23. The UniGene set serves as a source of mapping candidates and as a standard to compare and screen new EST submissions. ESTs are screened against each other to determine those likely to be derived from the same gene and sequences share statistically significant (predetermined threshold) DNA similarity (common patterns), and placed into the same cluster (NCBI News, page 3, lines 1-39). New EST submissions that do not match any sequences (predetermined threshold) in the UniGene set are considered (selected) new human genes and are

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organized into unique clusters to provide additional mapping candidates (NCBI News, page 3, last line, to page 4, line 3), as in instant claims 8 and 11.

24. UniGene screens all ESTs against existing functionally cloned GenBank entries to eliminate redundancies (NCBI News, page 3, lines 35-36). In this manner, the nearly 500,000 ESTs in dbEST have been reduced 10-fold to ~50,000 sequence clusters (create a new set of sequences) to be used for gene discovery (Benson et al., page 2, column 2, EST data §), as in instant claim 10.

25. “NCBI offers the BLAST family of search programs to perform fast searching with rigorous statistical methods for judging the significance of matches” (Benson et al., Page 5, column 1, lines 42-44). The inclusion of a reference by Altschul et al. is not being used as prior art, but only to expand on the inherent characteristics of BLAST as cited above.

26. In BLAST, statistical significance scores are calculated a set of probabilities for the occurrence of individual residues (at least one expected symbol), and for aligning pairs of residues (plurality of positions) (Altschul et al., page 405, column 2, §3. Results). BLAST measures well-defined mutation scores (occupied by any sequence character) and detects biologically significant sequence similarities (Altschul et al., page 404, column 1, lines 1-9), as in instant claim 6 and 7.

27. The choice of word length and threshold parameters determines the probability of hits yielded wherein hits are sequences with common patterns. If no common patterns are detected, the choice of word length and threshold parameters may be decreased to increase the probability of finding hits (common patterns) (Altschul et al., pages 406-408, The choice of word length and threshold parameters §), as in instant claim 12.

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28. GenBank is a part of the Entrez system (Abstract etc.). “The server/client version of Entrez operates with a client program on a user’s machine over the Internet connected to a server located at NCBI. Client programs for Macintosh, PC and UNIX computers can be obtained by downloading from ‘ncbi.nlm.nih.gov’ (Benson et al., Page 5, column 1, lines 26-30), the above disclosures anticipate the limitations of claims 23 and 25.

RESPONSE TO ARGUMENTS

29. On pages 6-10, Appellant argues that Benson et al. does not “teach or suggest discovering any patterns.” Appellant’s argument has been fully considered and found to be unpersuasive because the limitation of “discovering of a plurality of patterns” has not been explicitly defined in the instant specification. Therefore, without an explicit definition, the claim limitations and the claims as a whole have been given their broadest reasonable interpretation in light of the supporting disclosure. For example, on pages 8-11 of the instant specification, Appellant describes the claimed invention as directed to searching in an unsupervised manner to determine statistically significant common patterns between some or all of the family members. Each member comprises a sequence (e.g. DNA, proteins, etc.). The statistically significant and common patterns are determined by sequence alignments. Therefore, the disclosure of Benson et al. as cited below anticipates the limitations of claims 1-8, 10-12, 23 and 25 in regard to the limitation of “discovering of a plurality of patterns” as defined by the instant specification.

30. Specific to claim 4, Appellant argues that the sequences described in Benson et al. are not characterized, does not, in any way indicate that they are not aligned. It is noted that the

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limitation of “unaligned” in claim 4 is anticipated by Benson et al. via the citation of NCBI News (NCBI News, page 3, lines 1-35). UniGene comprises clusters of EST sequences wherein said EST sequences are not complete and have not been characterized (unaligned). These EST sequences started rolling into GenBank by the thousands and the problem was to organize the data in such a way that all representations of a single gene were collected in a single cluster (NCBI News, page 3, lines 1-35). The citation above represents unaligned sequences that are organized via sequence cluster. Therefore, the discussion of “uncharacterized” EST sequences in light of the clustering by sequence alignment in UniGene supports that Benson et al. via NCBI News describes the limitation of “unaligned” sequences. Therefore, the citation of NCBI News, page 3, lines 1-35 supports that Benson et al. anticipates the claimed invention as recited by claim 4.

31. Specific to claim 5, Appellant argues that Benson et al. does not teach or suggest “setting a predetermined number criteria.” It is noted that claim 5, line 2, recites the limitation of “if the candidate sequence comprises the predetermined number of patterns.” Benson et al. via NCBI News discloses new EST submissions that do not match any sequences (predetermined threshold) in the UniGene set are considered (selected) new human genes and are organized into unique clusters to provide additional mapping candidates (NCBI News, page 3, last line, to page 4, line 3). Further, ESTs are screened against each other to determine those likely to be derived from the same gene and sequences share statistically significant DNA similarity (common patterns) are placed into the same cluster (NCBI News, page 3, lines 1-35). The citation of “sequences share statistically DNA similarity” supports that Benson et al. describe at least two

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predetermined patterns, one from each sequence. Therefore, the citation above anticipates the limitation of “predetermined number of patterns” of claim 5.

32. Specific to claim 8, NCBI News discloses each member comprises a sequence (e.g. DNA, proteins, etc.). The statistically significant and common patterns are determined by sequence alignments (NCBI News, page 3, lines 35-39). New EST submissions that do not match any sequences (predetermined threshold) in the UniGene set are considered (selected) new human genes and are organized into unique clusters to provide additional mapping candidates (NCBI News, page 3, last line, to page 4, line 3), which anticipate the argued limitations.

33. Specific to claim 11, Appellant argues that “Nothing, therefore, Benson and/or NCBI News in any way indicates collecting statistically significant information, patterns or otherwise, e.g., in a composite descriptor.” It is noted that claim 11 does not recite the limitation of “collecting...e.g., in a composite descriptor.” As to the limitations recited in the instant claim 11, the citation of Benson et al. via NCBI News, page 3, last line, to page 4, line 3, as cited below anticipates claim 11.

34. Specific to claims 6 and 7, Appellant argues “BLAST does not anticipate discovering patterns common...a number of the patterns.” It is noted the argued limitation of “discovering a plurality of patterns” has been responded to above. Specific to the argument that “BLAST would not be a suitable program to determine whether certain patterns exist in a candidate sequence,” Appellant is invited to evidentiary support for an unsubstantiated opinion that is against what is well known in the art in regard to the use of BLAST for pattern searches.

35. Appellant argues "BLAST does not involve search criteria having one of either positions that each comprises... any sequence character." It is noted that claims 6 and 7 do not recite the argued "search criteria limitation." As for the limitations recited in claims 6 and 7, Benson et al. via Alschul et al. discloses statistical significance scores are calculated in BLAST for a set of probabilities for the occurrence of individual residues (at least one expected symbol), and for aligning pairs of residues (plurality of positions) (Altschul et al., page 405, column 2, §3. Results). BLAST measures well-defined mutation scores (occupied by any sequence character) and detects biologically significant sequence similarities (Altschul et al., page 404, column 1, lines 1-9).

CLAIM REJECTIONS - 35 USC § 103

36. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benson et al. (1997) taken with Kleffe et al. (1998).

BASIS FOR REJECTION

37. Benson et al. discloses the limitations to claims 1-8 and 10-12 as discussed above. Further, Benson et al. discloses GenBank comprising *Arabidopsis* sequences (page 2, column 1, line 1) is a major source of sequences for new gene discoveries (Benson et al., page 2, EST data §).

38. However, Benson et al. does not disclose the limitation of using a second-order Markov chain method, as in instant claim 9.

39. Kleffe et al. discloses an improvement for using second-order Markov chain method to predict gene structure (Abstract etc.). The algorithm of Kleffe et al. produces a set of alternative

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gene predictions that differ in the assignment of splice junctions (page 232, column 2, last paragraph). The method of Kleffe et al. requires the use of GenBank sequence information (page 233, column 1, Derivation of gene structures §). The second-order Markov chain method is used to determine the natural logarithm of the probability of a specific sequence (pattern) occur in the *Arabidopsis* sequences (pages 242-243, Appendix: Derivation of Markov models §), as in instant claim 9.

40. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement disclosed by Kleffe et al. and utilize the second-order Markov chain method in the method of Benson et al. for discovering new genes. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the gene discovery method of Benson et al. and Kleffe et al. with the second-order Markov chain method.

RESPONSE TO ARGUMENTS

41. Appellant argues that Kleffe et al. “reveal no teaching or suggestion of the concept of patterns.” As cited below, Kleffe et al. describes the second-order Markov chain method is used to determined the natural logarithm of the probability of a specific sequence (pattern) occur in the *Arabidopsis* sequences (pages 242-243, Appendix: Derivation of Markov models §). For a given sequence segment, the algorithm of Kleffe et al. produces a set of alternative gene predictions (patterns) that differ in the assignment of splice junctions (page 232, column 2, last paragraph). The citation of “set of alternative gene predictions” is reasonably consistent the disclosure of “patterns” in the instant specification on pages 8-11.

For the above reasons, it is believed that the rejections should be sustained.

CONCLUSION

42. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. The USPTO's official fax number is (571) 273-8300.

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45. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

46. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Respectfully submitted,

C. Dune Ly *[Signature]*
April 21, 2005

Conferees

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